UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency **Office of Pesticide Programs**

Antimicrobials Division (AD)

Monday, September 26, 2011

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 1677-185
DP Barcode: D391432
Product Name: Enviro San

From: Ian Blackwell, Biologist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

Through: Karen Hicks, Team Leader
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

To: Marshall Swindell, PM 33/ Karen Leavy
Regulatory Management Branch
Antimicrobials Division (7510P)

Applicant: Ecolab, Inc.

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Hydrogen peroxide	11.2
Peroxyacetic acid	15.2
Other Ingredient(s):	73.6
Total:	100.0

I BACKGROUND: EcoLab, Inc., has submitted two new acute toxicity studies to support the data requirements of their registered product, Reg. No. 1677-185. The registrants apparently submitted these studies to support precautionary labeling and PPE statements primarily for **use-dilutions** of this product. The Chemistry and Toxicology Team (CTT) cannot locate prior acute toxicity reviews of 1677-185 in EPA databases. PM Team 33 requested old acute toxicity reviews of 1977-185 from the registrants. The registrants provided three documents:

1. An 8/7/97 response to an acute toxicity data waiver request for Reg. Nos. 1677-158 and -159.
2. A 4/22/98 letter to Klenzade (Division of EcoLab, Inc.) concerning a review of toxicity data for Peroxy Compounds for Reg. No. 1677-159.
3. A 3/24/98 acute toxicity review of Reg. No. 1677-159 by SRRD (now PRD).

The results of that review were:

Acute Toxicity Profile of 1677-159 (3/24/1998)			
Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	427081-06	III	Acceptable
Acute Dermal Toxicity	None	I	Waived
Acute Inhalation Toxicity	None	?	Data Gap
Primary Eye Irritation	None	I	Waived
Primary Skin Irritation	None	I	Waived
Dermal Sensitization	None	N/A	Waived

The Product Science Branch (PSB) /Antimicrobials Division (AD) contractor, Computer Sciences Corporation (CSC) Systems and Solutions, LLC, conducted a primary review of these two studies. The Chemistry and Toxicology Team (CTT) conducted a brief secondary review to assure that the studies meet EPA/OPP criteria and assign toxicity categories.

II RECOMMENDATIONS:

1. The acute inhalation toxicity study is acceptable. However, this study has several deficiencies that EcoLab must report to the testing facility, IIT Research Institute. These study deficiencies are located in the attached Data Evaluation Review (DER).

2. CTT could not locate prior acute toxicity reviews of 1677-185. We do not know if any ever existed. It is *possible* that if the toxicity categories of the other four studies were determined in other studies, but, the reviews are not available. **The results of the two submitted studies will only apply to user exposure to the product at dilutions of 1:17.5 or more (e.g., 1:18, 1:19, etc.).**

3. CTT denies the registrants' request to cite acute toxicity data waivers (from 1677-159) to support the acute toxicity data requirements of EPA Registration Number 1677-185. CTT denies the waiver because one cannot cite an acute toxicity data waiver. For example, one product can receive primary and skin irritation waivers because it has a pH of 12.5 or more. A second product cannot cite that first product's pH. Pesticide products can only achieve acute toxicity waivers based upon their own physical and chemical (pH, viscosity, etc.) characteristics.

4. The Agency granted acute toxicity waivers for 1677-159. However, the reported pH of 1677-185 does not meet Agency guidelines for acute toxicity waivers based upon pH (below pH 2 or above 11.5). CTT noticed that the pH of 1677-185 is based upon a 1% solution of the registration product. If the registrants can demonstrate that a more concentrated solution of the product (greater than 1%) has a pH below 2, then CTT would have reason to reassess waivers of the primary eye and skin irritation studies.

5. CTT denies the request to cite the acute oral toxicity study from 1677-159 to support 1677-185. The formulas of the two products are too dissimilar to bridge from 1677-159 to 1677-185. One of the problems is that 1677-185 contains much more peroxyacetic acid than 1677-158.

The acute toxicity profile for Registration Number 1677-185 is currently:

Acute Toxicity Profile for **Use-Dilution** of 1677-185			
Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	None	?	Data Gap
Acute Dermal Toxicity	None	?	Data Gap
Acute Inhalation Toxicity	485118-02	IV	Acceptable
Primary Eye Irritation	None	?	Data Gap
Primary Skin Irritation	485118-01	IV	Acceptable
Dermal Sensitization	None	?	Data Gap

III LABELING:

1. CTT cannot prescribe a Signal Word or regular Precautionary Statements or First Aid statements for 1677-185 due to a lack of acute toxicity data. Using the current acute toxicity profile, we can only say that for **use-dilutions of the product of 1:17.5 or more**, there will be no First Aid or Precautionary Statements required for acute inhalation toxicity or primary skin irritation. This **does not** apply to any of the other four acute toxicity disciplines, and, does not apply to the undiluted product.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OPPTS 870.1300)
(NOSE-ONLY EXPOSURE)

Product Manager: 33
MRID No.: 485118-02

Reviewer: CSC and Ian Blackwell
Completion Date: November 16, 2010
Project No.: 2271 SN3

Testing Laboratory: IIT Research Institute, Chicago, IL
Author: Dennis M. Sullivan, M.S., D.A.B.T.

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study was conducted in accordance with U.S. EPA GLP standards (40 CFR Part 160).

Test Material: Enviro San, Batch #: J070891 / Clear liquid

Note: According to the study protocol provided in Appendix A, the product was applied diluted (i.e., 57 grams of the product and 1,000 grams of ASTM-1 water; a 1:17.5 dilution).

Species: 10 Rats; Sprague-Dawley derived [Crl:CD(SD)IGSBR]
Sex: 5 Males and 5 Females
[The laboratory did not report whether females were nulliparous and non-pregnant.]
Age: Young adult (~8 weeks old upon receipt; 9 weeks old on Day 1 prior to exposure)
Weight: Males: 260-285 grams; Females: 211-229 grams; on Day 1 prior to exposure
Source: Charles River Laboratories, Inc., Portage, MI
Housing: Temperature Range: 23-26°C
Humidity Range: 48-72%
Photoperiod: 12-hour light/12-hour dark cycle
Acclimation: 1 week

Concentration:

Group	Gravimetric Exposure Concentration (mg/L)	Nominal Concentration (mg/L)
I	2.05	21.7

Summary:
1. **LC_{50} (mg/L) 4-hr exposure**: >2.05 mg/L in male and female rats

2. **The estimated 4-hr acute inhalation LC_{50} of a 1:17.5 dilution of Enviro San is greater than 2.05 mg/L in male and female rats.**

3. **Average MMAD**: 1.77 μm

4. **Toxicity Category**: IV (use-dilution) **Classification**: Acceptable

Procedure (Deviations from 870.1300):

- The laboratory reported the following protocol deviation to Protocol Section 9.g. Environmental Controls: "The room temperature was 25.6°C on July 14, 2010."
- The laboratory reported the following protocol deviation to Protocol Section 9.g. Environmental Controls: "The room relative humidity was 72% on July 15, 2010."
- The guidelines specify that females used in the study should be nulliparous and non-pregnant. The laboratory did not specify whether females were nulliparous and non-pregnant.
- The guidelines state that the animals should be acclimated and heat stressed minimized. The laboratory did not indicate whether animals were acclimated to exposure conditions and heat stress minimized.
- The guidelines state that three to four measurements should be taken during exposure if chamber concentrations and MMAD values taken during the trial run measurements are not within 10 percent of each other. Information about trial run studies was not provided. The laboratory conducted only two sample measurements during the test, instead of the three to four measurements recommended in the guidelines.
- The guidelines state that a description of the exposure apparatus, including design, type, and dimensions, should be reported. The exposure apparatus was identified as Chamber 1 of Inhalation Laboratory IX of the IITRI Inhalation Facility. The exposure apparatus was described as having a 64-port, flow-past, nose-only inhalation exposure chamber. The laboratory did not provide dimensions of the exposure apparatus.
- The guidelines state that particle size distribution should be reported. The laboratory stated that particle size distribution was determined using a QCM Cascade Impactor, but did not report particle size distribution data.
- [Note to EPA Reviewer: The Certificate of Analysis suggests that the undiluted product contains concentrations of the active ingredients that are less than the nominal concentrations of the active ingredients (and less than the standard lower certified limits for the active ingredients).]
- [Note to EPA Reviewer: The product was tested at a 1:17.5 dilution, which appears to correspond to the use solution described on the product label for sterilizing food packaging materials (i.e., a 5.0 ounces/1.0 gallons use solution; a 1:25.6 use solution). Other less concentrated use solutions are identified on the product label.]

Results:

Reported Mortality

Exposure Concentration (mg/L)	Number Dead / Number Tested		
	Males	Females	Combined
2.05	0 / 5	0 / 5	0 / 10

Chamber Atmosphere:

The geometric standard deviation (GSD) range of the test atmosphere was 1.81 to 1.86.

Chamber Environment during Exposure

Exposure Level (mg/L)	2.05
Chamber Volume (L)	not reported (64-port)
Average Total Airflow Volume (Lpm)	24.22
Air Changes Per Hour	not reported
Mean Oxygen Content (%)	22.6
Temperature Range (°C)	23.0-24.4
Relative Humidity Range (%)	99

Clinical Observations:

No mortality occurred during the observation period.

The observed clinical signs included wet inguinal fur, salivation, redness around the eyes (one male only), and redness around the nose fur. Animals were asymptomatic by Day 7. Wet inguinal fur and salivation were considered to have resulted from the animals being in the exposure tubes; however, redness around the nose fur was considered compound-related.

All animals gained weight during the post-exposure observation period, with the exception of one female animal that lost 1 gram of weight between Day 8 and Day 15.

Gross Necropsy Findings:

No gross lesions were observed in any of the animals at terminal necropsy.

DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (OPPTS 870.2500)

Product Manager: 33
MRID No.: 485118-01

Reviewer: CSC and Ian Blackwell
Completion Date: September 8, 2010
Project No.: 2271 SN1

Testing Laboratory: IIT Research Institute, Chicago, IL
Author: Dennis M. Sullivan, M.S., D.A.B.T.

Quality Assurance (40 CFR §160.12): A Quality Assurance (QA) statement was included. A statement of Good Laboratory Practice (GLP) compliance was included stating that this study was conducted in accordance with U.S. EPA GLP standards (40 CFR Part 160), with the following exception: analysis of the dose formulation for concentration was not performed.

Test Material: Enviro San, Batch #: J070891 / Clear liquid

Dosage: 0.5 mL (applied diluted; 57 grams of the product and 1,000 grams of purified water; a 1:17.5 dilution)

Species: 3 Rabbits; New Zealand White
Sex: Females
[The laboratory did not report whether females were nulliparous and non-pregnant.]
Age: Adult (~3 months old upon receipt; ~4.5 months old on date of selection for study)
Weight: Information not provided (and not required)
Source: Kuiper Rabbit Ranch, Gary, IN
Housing: Temperature Range: 20.7-23.0°C
Humidity Range: 56-68%
Photoperiod: 12-hour light/12-hour dark cycle
Acclimation: 47 days

Summary:

1. **Toxicity Category**: IV (for use-dilution)

2. **Classification**: Acceptable

Procedure (Deviations from 870.2500):

- The laboratory reported the following protocol deviation to Protocol Section 9.e. Food: "The Rabbits were fed Harlan Rabbit Diet #2030 (a lower fiber diet)." No adverse effect would be expected on the overall integrity of the study.
- The laboratory reported the following protocol deviation to Protocol Section 9.a. Model: "The rabbits were not weighed prior to dosing as the animals were

adults and body weight is not an important criteria for an Acute Dermal Irritation Study as the physical examination of the animals." No adverse effect would be expected on the overall integrity of the study.

- [Note to EPA Reviewer: The Certificate of Analysis suggests that the undiluted product contains concentrations of the active ingredients that are less than the nominal concentrations of the active ingredients (and less than the standard lower certified limits for the active ingredients).]
- [Note to EPA Reviewer: The product was tested at a 1:17.5 dilution, which appears to correspond to the use solution described on the product label for sterilizing food packaging materials (i.e., a 5.0 ounces/1.0 gallons use solution; a 1:25.6 dilution). Other less concentrated use solutions are identified on the product label.]

Results:
No animals died or were found moribund during the study.

Following an exposure period of 4 hours, no signs of edema or erythema/ eschar formation were observed in any of the three animals used in the study at any scoring interval.

According to the Draize descriptive ratings for skin irritancy, the Primary Dermal Irritation Index for a 1:17.5 dilution of Enviro San (based on the 24- and 72-hour scoring intervals) is 0.00. Therefore, under these study conditions, a 1:17.5 dilution of Enviro San was non-corrosive and a non-irritant.

Incidence of Irritation

Time after Patch Removal	Erythema and Eschar	Edema
1 hour	0 / 3	0 / 3
24 hours	0 / 3	0 / 3
48 hours	0 / 3	0 / 3
72 hours	0 / 3	0 / 3

Individual Skin Irritation Scores

Animal No.	Sex	Erythema and Eschar / Edema			
		Time After Patch Removal			
		1 hour	24 hours	48 hours	72 hours
173	**F**	0 / 0	0 / 0	0 / 0	0 / 0
174	**F**	0 / 0	0 / 0	0 / 0	0 / 0
175	**F**	0 / 0	0 / 0	0 / 0	0 / 0
Total		0 / 0	0 / 0	0 / 0	0 / 0
Mean		0.0 / 0.0	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0

Summary of Skin Irritation Scores[1]

	Time After Patch Removal			
	1 hour	24 hours	48 hours	72 hours
Erythema/ Eschar	0.0	0.0	0.0	0.0
Edema	0.0	0.0	0.0	0.0
TOTAL (PDI)[2]	0.0	0.0	0.0	0.0

[1]Average values for three rabbits

[2]PDI = Average Erythema/ Eschar + Average Edema